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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/281,528	03/30/99	ROBERTSON D	5051-425

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EXAMINER	
KAUSHAL, S	
ART UNIT	PAPER NUMBER
1633	15

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Offic Action Summary	Application No. 09/281,528	Applicant(s) ROBERTSON, DOMINIQUE	
	Examiner Sumesh Kaushal	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,9,11-16,18,19,21,31,32 and 35-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8,9,11-16,18,19,21,31,32 and 35-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

Applicant's response filed on 06/19/01 have been fully considered but is found unpersuasive for the same reasons of record as set forth in the earlier office action (Paper No.11, 01/16/01).

The applicant cancels claims 7, 10, 17, 20, 22-30 and 33-34, amends claims 1, 4-6, 8-9, 11-12, 16, 18-19, 21 and 31 and newly files claims 36-60. Claims 1-6, 8-9, 11-16, 18-19, 21, 31-32 and 35-60 are pending and are examined in this office action.

Election/Restrictions

This application contains claim 35 drawn to an invention nonelected with traverse in Paper No. 7. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 1-6, 8-9, 11-16, 18-19, 21, 31-32 and 35-60 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had **possession of the claimed invention** for the same reasons of record as set forth in the official action mailed on 01/16/01.

The invention as claimed encompasses a geminivirus silencing vector, a DNA construct comprising geminivirus genome, a geminivirus silencing vector comprising TGMV genome and/or a geminivirus silencing vector comprising ACMV genome, which contains hetrologous DNA that have at least 60% sequence similarity to a gene endogenous to a plant. The invention as claimed encompass a plant cell and a plant comprising a geminivirus silencing vector, wherein the vector comprises geminivirus genome, which contains hetrologous DNA that have at least 60% sequence similarity to any and all gene endogenous to any and all plants. The claims are drawn to the geminivirus silencing vectors or a DNA construct wherein the hetrologous DNA sequences (with 60% sequence similarity to a gene endogenous to a plant) in sense or antisense orientation. In addition the claims are drawn to a method of silencing the expression of an endogenous plan gene in a plant cell via a geminivirus silencing vector or a DNA construct encoding a hetrologous DNA which have 60% similarity to a gene endogenous to a plant.

The applicant argues that the out standing rejection provide no objective evidence as to why one skill in the art would not find that the inventors had possession of the claimed invention in view of the disclosure in the specification (response: page 10). The applicant further argues that the present specification gives extensive guidance as to what other gene sequences and what other plants may be used to carry out the present invention (response: page 11, ¶2). The applicant further argues that the claims have been amended to recite at least 60% sequence similarity between the hetrologous sequence carried by silencing vectors and endogenous plant gene to be silenced (response: page 11, ¶4).

However, this is not found persuasive because the scope of invention as claimed encompasses any and all geminivirus vectors encoding sequences capable of silencing any all genes in any and all plants species and with at least 60% similarity to the endogenous gene of interest. At best the specification as filed only disclosed the silencing of magnesium chelatase gene and luciferase gene in N. benthamiana by particle bombardment using TGMV. The specification fails to disclose all geminivirus vectors or genomes thereof. Furthermore, the specification fails to disclose any and all hetrologous DNA sequences having at least 60%

sequence similarity with any and all genes obtained from any and all plants. Furthermore, the specification fails to disclose that a hetrologous DNA sequences having at least 60% sequence similarity with any and all genes obtained from any and all plants species would silence the expression of an endogenous gene in a plant.

The earlier office action clearly states that possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention Pfaff v. Wells Electronics, Inc 48 USPQ2d 1641, 1646 (1998). In addition, one cannot describe what one has not conceived. *See Fiddes v. Baird, 30 USP2d 1481 at 1483*. In Fiddes, claims directed to a mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence (*See Fiddes v. Baird, 30 USP2d 1481 at 1483)*. At best specification only disclosed the silencing of magnesium chelatase gene and luciferase gene in N. benthamiana by particle bombardment using a TGMV vector, which does not represent the genus of geminiviruses and any and all plant genes as claimed. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim. Therefore, the burden shifts to applicant to establish that applicants were in the possession of the claimed genus.

Claim 1-6, 8-9, 11-16, 18-19, 21, 31-32 and 35-60 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the silencing of the magnesium chelatase gene and the luciferase gene in N. benthamiana using a TGMV vector, does not reasonably provide enablement for any and all geminivirus silencing vector comprising any and all geminivirus genome, a DNA construct comprising any and all geminivirus silencing vectors, wherein the genome contains hetrologous DNA which have at least 60% sequence similarity to any and all genes endogenous to any and all plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to use the invention **commensurate in scope** with these claims for the same reasons of record as set forth in the official action mailed on 07/16/01.

The invention as claimed encompasses any and all geminivirus silencing vectors, a DNA construct comprising any and all geminivirus genomes, a geminivirus silencing vector comprising TGMV genome and/or a geminivirus silencing vector comprising ACMV genome, wherein the vectors contain hetrologous DNA that have at least 60% sequence similarity to a gene endogenous to a plant. The invention as claimed further encompass a plant cell comprising a geminivirus silencing vector, wherein the vector comprises geminivirus genome, which contains hetrologous DNA that have at least 60% sequence similarity to any and all gene endogenous to any and all plants. The claims are further drawn to the geminivirus silencing vectors or a DNA construct wherein the hetrologous DNA sequences (with 60% sequence similarity to a gene endogenous to a plant) in sense or antisense orientation. In addition the claims are drawn to a method of silencing the expression of an endogenous plan gene in a plant cell via a geminivirus silencing vector or a DNA construct encoding a hetrologous DNA which have 60% similarity to a gene endogenous to a plant.

The applicant argues that one skill in the art would could make and use the invention without undue amount of experimentation and the application provides substantial guidance as how the invention may be carried out with other genes and other plant species (response: page 12, ¶2-3). Citing Peele et al who teaches silencing of PCNA gene in N. Benthamina using a TGMV vector and Turange et al who teaches silencing of magnesium chelate gene in Arabidopsis using CLCV vector, the applicant argues that invention as claimed is enabled to the breadth as claimed (response: page 13, ¶2-3). Considering the unpredictability in the art in view of Covey et al and Kjemtrup et al (ref. cited in the earlier office action) the applicant argues that "patentability does not require an understanding of the molecular basis of the invention" (response: page 13, ¶4). The applicant further argues that it is not necessary that the invention be completely predictable to satisfy the enablement requirement (response: page 14, ¶1). The applicant admits that "it is possible that there are some embodiments of invention that are

inoperative but these may be determined with no more than routine experimentation (response: page 15, ¶3).

However, this is not found persuasive because the invention as claimed encompass any and all geminivirus vectors or genome thereof which encodes a hetrologous DNA sequence from any and all plant genes with 60% similarity. At best the specification as filed only disclosed the silencing of magnesium chelatase gene and luciferase gene in N. benthamiana by particle bombardment. It is unclear how one skill in the art would use the invention as claimed which encompass any and all geminiviral vectors encoding any and all plant genes, which have 60% similarity across any and all pant species.

The earlier office action clearly states that although gene silencing in plants as a phenomenon has long been recognized the gene silencing in plant yet incompletely understood because little is known about the relationship between nuclear and cytoplasmic events during gene silencing (Covey et al). Furthermore, considering the unpredictability of transgene silencing in plants the understanding of the molecular basis of the invention is germane to invention as claimed. Each virus is known to produce a characteristic pattern of silencing and there are variations in the tissue specificity, which depends upon the mode of action of the suppressor and the component of gene silencing mechanism (Voinet et al, PNAS 96(24):14147-14152, 1999). Furthermore some genes escape inactivation despite the presence of a homologous partner due to subset of transformants in which both the transgene and homologous resident (trans)gene continue to be expressed (Neuhuber et al). The invention as claimed also encompass gene silencing using episomes. The earlier office action clearly states that episomal gene silencing is not uniform in all plants and is dependent upon episomal copy number. Kjemtrup et al states that episomal gene silencing is unpredictable because to understand the relationship between episomal DNA and gene silencing, one need to determine if silencing nuclear genes could be triggered by homologous sequences carried by a geminivirus episome. Although, Kjemtrup et al provide evidence that they can down-regulate the expression of two genes in plants, they clearly state that there application of a geminvirus based vector to episomally silence a gene is a new area of endeavor.

In addition, Peele et al (The Plant J. 27(4):1-11, 2000) teaches that silencing of genes in plant varies with the tissue type and the gene of interest. For example, silencing of PCNA gene in meristematic tissue was not as uniform as loss of chlorophyll following su silencing (page 8, col.2 para.2). The invention as claimed encompass the use of a hetrologous DNA having at least 60% similarity, which means that 40% nucleotide sequences are not identical to the gene of interest. Therefore, it is unclear how any and all genes or variants thereof (60% similarity) selected from any and all plants would result in the silencing of the genes and it variants as claimed. Furthermore, geminiviruses genome has limited capacity to carry a foreign DNA sequence. For example, TGMV can carry a fragment of up to 800bp its genome to stably propagate and transcribe the gene of interest (Peele, page2, col.1 para.3). It is unclear how one skill in the art would select the minimum segment and/or its variant from the genus as claimed that would result in the silencing of the gene of interest

Thus it is unclear how one skill in the art would use the invention as claimed without excessive and undue amount of experimentation. The amount experimentation required would include making and testing any and all gene sequences from any and all species of plants that have at least 60% homology to any and all gene endogenous to any and all species of plant. In addition the experimentation required would further include use of DNA variants (as claimed) in silencing of any and all endogenous gene of any and all species of plants.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-9,11-16, 18-19, 21, 31-32, 35-41, 44-45, 48-49 and 50-61 rejected under 35 U.S.C. 102(b) as being anticipated by Kridl et al (US 5589379, 1996).

Kridl teaches a geminivirus-base gene expression system for obtaining controlled expression of a nucleic acid fragment of interest (abstarct). Kridl teaches a vector in which the coat protein ORF has been replaced by a hetrologous coding sequence and the hetrologous coding sequence is expressed from the coat promoter (col.2, line 47-60, col.4 line 22-38). The cited art further teaches a vector that comprises tissue specific transcription regulatory sequences (col.9 line 55-67). The cited art teaches that hetrologous nucleic acid of interest include open reading frame encoding a polypetide, non-coding leader sequences, or a sequence where complementary sequence inhibits transcriptin, messenger RNA processing (col.11, line 11-26). Furthermore, the cited art teaches the inhibition of expression of one or more endogenous gene products in a plant using an anti-sense nucleotide sequence (col.12, line 1-23). The cited art teaches the use of geminivirus vector for a controlled phenotypic expression of nucleic acid of interest (col.16, line 29-43). In addition the cited art teaches African Cassava mosaic virus vector wherein the coding sequence for the coat protein gene is deleted and replaced by a herologous DNA seqeunce (col.19-22). Thus the invention as claimed is clearly anticipated by the cited prior art.

Conclusion

No claims are allowed.

Claim 35 is objected to because of the following informalities: The instant claim depends upon claims 22-24, which were canceled by the applicant in response filed on 06/19/01. Appropriate correction is required.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-

6838. The examiner can normally be reached on Monday-Friday from 9:00 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Deborah Clark can be reached on (703) 305-4051. The fax-phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Tracey Johnson, whose telephone number is (703) 308-0377.

If the claims are amended canceled and/or added the applicants are required to follow Amendment Practice under 37 CFR § 1.121 *(http://www.uspto.gov)* and A CLEAN COPY OF ALL PENDING CLAIMS IS REQUESTED to facilitate further examination.

SUMESH KAUSHAL
PATENT EXAMINER

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PATENT EXAMINER